PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	25 JUL 2008
Applicant's or agent's file reference 74841-A/PCT	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US06/28565	21 July 2006 (21.07.2006)	22 July 2005 (22.07.2005)

International Patent Classification (IPC) or both national classification and IPC

IPC: **A61K 39/42**(2006.01);**C07K 16/00**(2006.01);**A01N 61/00**(2006.01)
USPC: 424/148.1,160.1;530/388.35;514/1

Applicant

PROGENICS PHARMACEUTICALS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	08 June 2008 (08.06.2008)	J.S. Parkin Telephone No. (571) 272-0500

Form PCT/ISA/237 (cover sheet) (April 2007)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US06/28565

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-104	YES
	Claims NONE	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-104	NO
Industrial applicability (IA)	Claims 1-104	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-46 lack an inventive step under PCT Article 33(3) as being obvious over Olson et al. (2003). Olson and colleagues provide a humanized antibody, designated PRO-140, that meets all of the claimed limitations. This antibody was utilized in the treatment of HIV-1 infection. The administration of this Mab with a known antiviral agent was also disclosed. This teaching does not specifically disclose reductions in viral load as a result of administration of the compound. However, one of ordinary skill in the art would reasonably expect a known antiviral that inhibits viral fusion events to inhibit viral replication thereby leading to a reduction in viral load. Accordingly, the claims lack an inventive step of the prior art.

Claims 47-104 lack an inventive step under PCT Article 33(3) as being obvious over the combined teachings of Olson et al. (2002,2003), Johnson et al. (2002), and Flentge et al. (2005). The claims are directed toward methods for reducing the HIV-1 viral load by administering compositions comprising Mabs (e.g., PA-14, PRO-140) in combination with other known antivirals (e.g., CCR5 inhibitors; protease inhibitors; fusion inhibitors; etc.). Olson et al., (2002) and (2003), provide anti-HIV compounds and methods of treating/inhibiting HIV viral replication by administering PA-14 and PRO-140, respectively. These teachings do not disclose the administration of these compounds with other art-recognized antivirals. However, both Johnson et al. (2002) and Flentge et al. (2005) provide pharmaceutical compositions comprising various antiviral compounds, including the known CCR5 inhibitors SCH-D, UK-427857, TAK-779, and GW873140. These teachings do not disclose compositions comprising both antivirals and therapeutic Mabs. However, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to combine known antivirals and neutralizing Mabs into a single composition or treatment regimen to facilitate the inhibition of viral replication and reduce the opportunity for viral escape.

Claims 1-104 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.